REMARKS

Claims 1-12. 18-28, 34-43, 49-52, 57-60, 65-68 and 73-75 are pending in the present application. Applicants have amended claims 1, 2, 4, 5-12, 18, 19, 21-28, 34-43, 49-52, 57-60, 65-68 and 73 to replace the term "pluronic L61" with the term "poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) having approximately 10% ethylene oxide by weight and having an average molecular weight of propylene oxide block of approximately 1800." The two terms have been used interchangeably by BASF, the manufacturer of Pluronic L61 and by Sigma-Aldrich. For your convenience, a copy of the supporting documents for such a replacement is enclosed. Applicants respectfully submit that these amendments are fully supported and do not raise any issue of new matter. Accordingly, entry of the present Amendment is respectfully requested. Upon entry of the present Amendment, claims 1-12. 18-28, 34-43, 49-52, 57-60, 65-68 and 73-75 will be under examination.

REJECTION OF CLAIMS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1-12, 18-28, 34-43, 49-52, 57-60, 65-68 and 73-75 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Office Action objects to the use of the phrase "Pluronic L61" as allegedly being a trademark or trade name.

Applicants have amended the claims by replacing the objected term "pluronic L61" with term "poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) having approximately 10% ethylene oxide by weight and having an average molecular weight of propylene oxide block of approximately 1800." Therefore, the ground of objection is moot.

REJECTION OF CLAIMS UNDER 35 U.S.C. §103

Claims 1-12, 18-28, 34-43, 49-52, 57-60, 65-68 and 73-75 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Curatolo et al., U.S. Patent No. 5,605,889

("Curatolo") in combination with the International Patent WO 99/39731 ("the International Patent").

Applicants respectfully disagree with this ground of rejection. Applicants respectfully point out that the Office Action fails to establish a *prime facie* case of obviousness under the standard of M.P.E.P. § 2142 which states that:

> to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.

The Office Action does not meet at least the first and third requirements. Specifically, Curatolo disclosed oral delivery of azithromycin. The International Patent disclosed oral delivery of a variety of biological agents, including proteins, peptides and the likes in the presence of various block co-polymers. The International Patent further defined biological agents as including hundreds of antifungal and antibacterial drugs. However, the International Patent does not specifically disclose azithromycin and there is no teaching or suggestion to combine Curatolo and the International Patent. Even assuming that they can be combined, such a combination does not provide any specific teaching, suggestion or motivation to a skilled artisan on how to obtain the claimed method of increasing the bioavailability of azithromycin, comprising co-administering, to a mammal in need of such treatment, a combination of azithromycin and poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) having approximately 10% ethylene oxide by weight and having an average molecular weight of propylene oxide block of approximately 1800.

With regard to the Office Action's statement that erythromycin was disclosed in the last line of page 36, Applicants would like to point out that erythromycin is not azithromycin.

Applicants further enclose a copy of a Declaration under 37 C.F.R. 1.132 which was filed in connection with the prosecution of U.S. Serial No. 08/328,977 to show that erythromycin and azithromycin have different properties. Even assuming that they are the same, there was still no specific teaching or suggestion on how to choose erythromycin from a list of hundreds of "biological agents," and then choose poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) having approximately 10% ethylene oxide by weight and having an average molecular weight of propylene oxide block of approximately 1800 among numerous block co-polymers to obtain the claimed method. The Patent Office seems to have used hindsight reconstruction prohibited by M.P.E.P. § 2143.01 which states that the "suggestion or motivation" criteria must be satisfied from the disclosure of the prior art reference or from the knowledge of persons skilled in the art, not by the use of hindsight in view of the present application (emphasis added). Therefore, the Office Action does not satisfy the first criteria for establishing a *prime facie* case of obviousness under M.P.E.P. § 2143.01.

In this case, even further assuming that Curatolo and the International Patent can be combined, the combination does not disclose "all the claim limitations." Specifically, Curatolo and the International Patent do not specifically disclose the use of azithromycin and poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) having approximately 10% ethylene oxide by weight and having an average molecular weight of propylene oxide block of approximately 1800. Therefore, the Office Action fails to satisfy the third criteria for establishing a *prime facie* case of obviousness under the M.P.E.P. § 2143.01.

Moreover, the International Patent does not provide any indication as to which drug on its list of hundreds of "biological agents" can achieve good delivery results when used with block co-polymers, let alone suggesting the use of a drug not on its list. Let's further assume that azithromycin, together with all the drugs known to human as of the filing date of the present application, are listed in the International Patent, this rejection is still an impermissible "obvious to try" rejection. As stated *In re O'Farrell*:

> The admonition that "obvious to try" is not the standard under § 103 has been directed mainly at two kinds of error. In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.

7 U.S.P.Q. 2d 1673, 1681 at 1681 (Fed. Cir. 1988) (citations omitted).

It is clear that this rejection is within the first of these two types of errors in obviousness rejection. Therefore, claims 1-12, 18-28, 34-43, 49-52, 57-60, 65-68 and 73-75 are nonobvious over Curatolo and the International Patent. Accordingly, reconsideration and withdrawal of this ground of rejection are respectfully requested.

In addition, as shown in Dr. Steve Sutton's declaration, Applicants have achieved superior results by using azithromycin and poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) having approximately 10% ethylene oxide by weight and having an average molecular weight of propylene oxide block of approximately 1800. The presence of poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) having approximately 10% ethylene oxide by weight and having an average molecular weight of propylene oxide block of approximately 1800 increased the beagle dog's exposure to azithromycin by 121-240% as measured by jugular AUC_{0-24}. Therefore, the pending claims on the combination of azithromycin and poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) having approximately 10% ethylene oxide by weight and having an average molecular weight of propylene oxide block of approximately 1800 are nonobvious over the disclosure of Curatolo and the International Patent as "superiority of a property shared with the prior art is evidence of nonobviousness," M.P.E.P. § 716.02 (a). Accordingly, reconsideration and withdrawal of this ground of rejection are respectfully requested.

CONCLUSION

In view of the amendments and the remarks, early and favorable consideration of all pending claims are respectfully requested.

It is believed that no fee is deemed necessary in connection with the filing of the present Amendment. However, if any fees are required, the Commissioner is hereby authorized to charge any such fees to our Deposit Account No. 16-1445.

Respectfully submitted,

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